

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

To:

Miles, John S.  
ERIC POTTER CLARKSON  
Park View House  
58 The Ropewalk  
Nottingham NG1 5DD  
GRANDE BRETAGNE

COMUS	PARTNER
28 FEB 2001	
ACTIONED BY:	

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year) 26.02.2001

Applicant's or agent's file reference  
ICOW/P21725PC

### IMPORTANT NOTIFICATION

International application No.  
PCT/GB99/03302

International filing date (day/month/year)  
15/10/1999

Priority date (day/month/year)  
15/10/1998

Applicant  
IMPERIAL COLLEGE INNOVATIONS LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
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REC'D 28 FEB 2001

WIPO

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ICOW/P21725PC	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/03302	International filing date (day/month/year) 15/10/1999	Priority date (day/month/year) 15/10/1998
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant IMPERIAL COLLEGE INNOVATIONS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

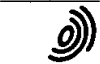

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  10/05/2000	Date of completion of this report  26.02.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Perez, F  Telephone No. +49 89 2399 7338 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03302

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

**Description, pages:**

1-57 as originally filed

**Claims, No.:**

1-43 as originally filed

**Drawings, sheets:**

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/03302

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-43 (see details).

because:

☒ the said international application, or the said claims Nos. 1-4, 29-31, 41 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-3, 29-36, 41-42, are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-2, 29-36, 41-42 (in part), 5-28, 37-40, 43 (completely).

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03302

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Novelty (N)	Yes:	Claims	30, 34-36, 42
	No:	Claims	1-4, 29, 31-33, 41
Inventive step (IS)	Yes:	Claims	30, 34-36, 42
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-4, 29-31, 35-36, 41 (see separate sheet); 32-34, 42 YES
	No:	Claims	

2. Citations and explanations  
**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB99/03302

**Re Item I**

**Basis of the report**

The attention of the applicant is drawn to the fact that this report is based, as requested in the Demand, on the international application documents as originally filed on 28 October, 1999. The amended version received with the letter dated 20 December, 1999 (rule 91 PCT) has not been taken into account.

**Re Item III**

**Non-establishment of report with regard to novelty, inventive step and industrial applicability**

**Claims 1-4, 29-31, 41** relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Ageing is not considered a disease, nevertheless weight loss is a factor for increased mortality. Consequently, treating weight loss (independently of its origin) is considered as a method of treatment. Therefore claims 35-36 are considered to relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34.4(a)(i) PCT).

The international search report is restricted to claims 1-2, 29-36, 41-42 (in part) and 3-4 (complete). **Claims 1-2, 29-36, 41-42 (in part) 5-28, 37-40, 43 (complete)** were not searched for the reason given on PCT/ISA/210. Consequently, International Preliminary Examination will not be carried out in respect of the subject-matter which was not searched (Rule 66.1(e) PCT).

With regard to PCT/ISA/210, **claims 1-3, 29-36, 41-42** relate to subject-matter considered by this Authority to be unclear and/or not sufficiently disclosed (Articles 5 and 6 PCT). Consequently, an opinion will be formulated only for searched subject-matter, namely subject-matter related to compounds explicitly mentioned in the examples and claim 4 (Article 34.4(a)(ii) PCT).

**R Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB99/03302

**industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

**D1:** HUANG ZHENWEN, LIU RUIYUN ET AL. ZHONGHUA XINXUEGUANBING ZAZHI, (1996) VOL. 24, NO. 1, PP. 12-15.

**D2:** ANKER S D ET AL. CURRENT OPINION IN CARDIOLOGY, (1999 MAY) 14 (3) 211-6. REF: 62.

**D3:** JP 09 071586 A (YAMANOUCHI OHARM CO LTD), 1997

**D4:** LEZA J.C. ET AL. REVISTA DE FARMACOLOGIA CLINICA Y EXPERIMENTAL, (1987) 4/4 (377-383).

**D5:** GREENBAUM L M ET AL. CANCER RESEARCH, (1983 JUN) 43 (6) 2584-7., 1983.

**D6:** DANERYD P ET AL. CANCER RESEARCH, (1998 DEC 1) 58 (23) 5374-9.

**D7:** GORTER R. ONCOLOGY, CH, S. KARGER AG, BASEL, vol. 5, no. 9, 1 September 1991, pages 13-17.

**D8:** GAGNON B ET AL. DRUGS, (1998 MAY) 55 (5) 675-88. REF: 136.

**D9:** WO 96 24373 A (SEARLE & CO ; MACLAUGHLAN TODD E (US); PEREZ ALFONSO T (US)) 15 August 1996.

D2 and D6 are P-documents. The priority of the present application has been found to be valid.

Novelty (Articles 33.1 and 33.2 PCT)

D1 discloses antialdosterone therapy for treating chronic congestive heart failure consisting in administering captopril alone or in combination with spironolactone, resulting in a reduction in excess weight loss. Therefore **claims 1-4, 29, 31-33, 41** lack novelty. Claims 30, 34-36, 42 relate to the treatment of either idiopathic cachexia or weight loss due to ageing with one of the compounds explicitly mentioned in the examples and claim 4. The use of antialdosterone therapy for the treatment of idiopathic cachexia or weight loss due to ageing is not disclosed in the prior art, rendering **claims 30, 34-36, 42** novel. It should also be noted that D3 discloses the use of antialdosterone therapy for the treatment of chronic heart failure and cirrhosis.

Inventive Step (Articles 33.1 and 33.3 PCT)

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB99/03302

Whereas the use of the compounds explicitly mentioned in the examples and claim 4 for the treatment of weight loss due to chronic heart failure is known from D1, this document does not suggest that this treatment could be applied to any weight loss due to an underlying disease. Therefore, **claims 30, 34-36, 42** can be regarded as inventive.

Industrial applicability (Articles 33.1 and 33.4 PCT)

For the assessment of the present **claims 1-4, 29-31, 35-36, 41** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VIII**

**Certain observations on the international application**

Claim 33 make reference to "an underlying disease" as defined in claim 28, but claim 28 does not further define this disease. Claim 33 was interpreted as making reference to claim 29.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
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CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

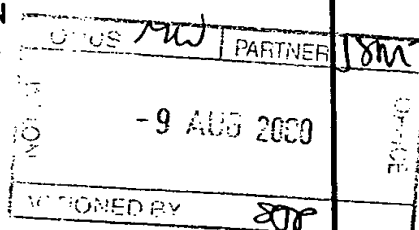
# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

ERIC POTTER CLARKSON  
Attn. Miles, John S.  
Park View House  
58 The Ropewalk  
Nottingham NG1 5DD  
UNITED KINGDOM



NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

08/08/2000

Applicant's or agent's file reference

ICOW/P21725PC

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/GB 99/ 03302

International filing date

(day/month/year)

15/10/1999

Applicant

IMPERIAL COLLEGE INNOVATIONS LIMITED et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Mike Iverstam

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/PEA/401).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>ICOW/P21725PC</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/GB 99/ 03302</b>	International filing date (day/month/year) <b>15/10/1999</b>	(Earliest) Priority Date (day/month/year) <b>15/10/1998</b>
Applicant  <b>IMPERIAL COLLEGE INNOVATIONS LIMITED et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.  
☐ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☒ Unity of invention is lacking (see Box II).

**4. With regard to the title,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. The figure of the drawings to be published with the abstract is Figure No.**

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☐ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 99/03302

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-4,29-30,35,36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
  
1-2,29-36,41-42 (partial) 3,4 (complete)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-2, 29-36, 41-42 (partial), 3,4,(complete).

Use of a compound which inhibits the effect of aldosterone, in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

2. Claims: 1-2, 29-36, 41-42 (partial), 5,6, (complete). (As far as not comprised in the previous invention).

Use of a chymase inhibitor in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

3. Claims: 1-2, 29-36, 38, 41-42 (partial), 7, 8 (complete). (As far as not comprised in the previous inventions).

Use of a cathepsin inhibitor in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

4. Claims: 1-2, 29-36, 38, 41-42 (partial), 9, 10 (complete). (As far as not comprised in the previous inventions).

Use of a beta receptor blocker in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

5. Claims: 1-2, 29-36, 38, 41-42 (partial), 11-12 (complete). (As far as not comprised in the previous inventions).

Use of an imidazoline receptor antagonist in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

6. Claims: 1-2, 29-36, 38, 41-42 (partial), 13-16 (complete). (As far as not comprised in the previous inventions).

Use of an alfa receptor agonist in relation to the treatment

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and the prevention of weight loss due to an underlying disease or to aging.

7. Claims: 1-2, 29-36, 38, 41-42 (partial),  
17-  
18 (complete). (As far as not comprised in the previous inventions).

Use of a ganglion blocking agent in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

8. Claims: 1-2, 29-32, 34-36, 38, 41-42 (partial),  
19-  
21 (complete). (As far as not comprised in the previous inventions).

Use of a compound with an effect on cardiovascular reflexes and reducing SNS activity such an opiate, in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

9. Claims: 1-2, 29-36, 38, 41-42 (partial),  
22 (complete). (As far as not comprised in the previous inventions).

Use of scopolamine in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

10. Claims: 1-2, 29-36, 38, 41-42 (partial),  
23-  
24 (complete). (As far as not comprised in the previous inventions).

Use of an endothelin receptor antagonist in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

11. Claims: 1-2, 29-36, 38, 41-42 (partial),  
25-  
26 (complete). (As far as not comprised in the previous inventions).

Use of a xanthine oxidase inhibitor in relation to the



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

treatment and the prevention of weight loss due to an underlying disease or to aging.

12. Claims: 1-2, 29-36, 38, 41-42 (partial),  
27 (complete). (As far as not comprised in the previous inventions).

Use of erythropoietin in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

13. Claims: 28, 37 (complete).

Use of electrically stimulating impulses in relation to the treatment and the prevention of weight loss due to an underlying disease or to aging.

14. Claims: 38,39,40,43 (complete).

Use of an agent which reduces sympathetic nervous system activity in relation to a treatment for enhancing exercise performance in a healthy patient.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

The wording "an agent which reduces sympathetic nervous system activity" is obscure and renders it difficult, if not impossible, to determine the matter for which protection is sought; for this reason, the present application fails to comply with the clarity and conciseness requirements of article 6 PCT.

Present claims 2-3,29-36,41,42 relate to compounds defined by reference to a pharmacological mechanism of action "compound which inhibits the effect of aldosterone" and "an aldosterone inhibitor". The definition of compounds by reference to a pharmacological mechanism in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to fully compare the parameters the applicant has chosen to employ with what is set out in the prior art. Present claim 1-4,29-36,41,42 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search for the first invention has been carried out for those parts of the claims which appear to be clear, concise, supported and disclosed, namely for the compounds explicitly mentioned in the examples and in claim 4, with due regard to the general idea underlying the application. Claim 33 probably should be dependent from claim 29.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 99/03302

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/165 A61K31/4178 A61K31/403 A61K31/585 A61K38/55

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS 'Online!  BIOSCIENCES INFORMATION SERVICE,  PHILADELPHIA, PA, US  AN=1996:426185,  HUANG ZHENWEN, LIU RUIYUN ET AL:  "Antialdosterone therapy in severe chronic  congestive heart failure."  retrieved from STN  XP002137362  abstract  &amp; ZHONGHUA XINXUEGUANBING ZAZHI, (1996)  VOL. 24, NO. 1, PP. 12-15.,  ---</p> <p style="text-align: center;">-/--</p>	<p>1-4, 29,  31, 32,  36, 41</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\* & \* document member of the same patent family

Date of the actual completion of the international search

10 May 2000

Date of mailing of the international search report

08.03.00

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Veronese, A

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 99/03302

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	ANKER S D ET AL: "Insights into the pathogenesis of chronic heart failure: immune activation and cachexia." CURRENT OPINION IN CARDIOLOGY, (1999 MAY) 14 (3) 211-6. REF: 62, XP000892578 the whole document	1-4, 29-36, 41,42
Y	DATABASE WPI Derwent Publications Ltd., London, GB; AN 1997-231178 XP002137363 "New bi-cyclic fuse imidazole derivatives used as aldosterone biosynthesis inhibitors, e.g. for treating chronic or congestive heart failure" & JP 09 071586 A (YAMANOUCHI OHARM CO LTD) , 1997 abstract	1-4, 29-36, 41,42
A	LEZA J.C. ET AL: "Buprenorphine suppresses weight loss and abstinence in morphine-dependent mice." REVISTA DE FARMACOLOGIA CLINICA Y EXPERIMENTAL, (1987) 4/4 (377-383)., XP000892647 page 380, column 1-2; figures 3,4	1-4, 29-36, 41,42
A	GREENBAUM L M ET AL: "Host cathepsin D response to tumor in the normal and pepstatin-treated mouse." CANCER RESEARCH, (1983 JUN) 43 (6) 2584-7., 1983, XP000892417 the whole document	1-4, 29-36, 41,42
P,A	DANERYD P ET AL: "Protection of metabolic and exercise capacity in unselected weight-losing cancer patients following treatment with recombinant erythropoietin: a randomized prospective study." CANCER RESEARCH, (1998 DEC 1) 58 (23) 5374-9., XP000877491 the whole document	1-4, 29-32, 34-36, 41,42
A	GORTER R: "MANAGEMENT OF ANOREXIA-CACHEXIA ASSOCIATED WITH CANCER AND HIV INFECTION" ONCOLOGY, CH, S. KARGER AG, BASEL, vol. 5, no. 9, 1 September 1991 (1991-09-01), pages 13-17, XP002054943 ISSN: 0030-2414 the whole document	1-4, 29-32, 34-36, 41,42

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 99/03302

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GAGNON B ET AL: "A review of the drug treatment of cachexia associated with cancer." DRUGS, (1998 MAY) 55 (5) 675-88. REF: 136, XP000892586 the whole document	1-4, 29-36, 41,42
A	WO 96 24373 A (SEARLE & CO ;MACLAUGHLAN TODD E (US); PEREZ ALFONSO T (US)) 15 August 1996 (1996-08-15) the whole document	1-4, 29-36, 41,42

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/GB 99/03302

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
JP 9071586	A	18-03-1997	NONE		
WO 9624373	A	15-08-1996	AU	5354196 A	27-08-1996
			BR	9604882 A	19-05-1998
			CA	2212713 A	15-08-1996
			EP	0808172 A	26-11-1997
			JP	11507012 T	22-06-1999